UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,647	04/21/2004	Sharat Singh	033.09-2US	5824

33603 7590 06/16/2006

MONOGRAM BIOSCIENCES
345 OYSTER POINT BLVD
SOUTH SAN FRANSISCO, CA 94080

EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 06/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/828,647	SINGH ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/21/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 4/21/2004 has been entered. Claims 21-30 are pending.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 21-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-30 of copending Application No. 10/779255. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 21-30 are drawn to a composition comprising a set of electrophoretic probe and a second reagent. The electrophoretic probe is selected from the group defined by the formula $[(D,M)\text{-}L]_k\text{-}T$, wherein T is a target-binding moiety specific for a target compound, K is an integer in the range of from 1-20, L is a cleavable linkage, D is a detection group and M is a mobility modifier and the second reagent is capable of generating an active species, singlet oxygen (recited in claim 30) to cleave the cleavable linkage, while claims 21-30

of copending Application No. 10/779255 are drawn to a probe set comprising a plurality of electrophoretic probes selected from the group defined by the same formula as the probe in the instant claims. Although the claims 21-30 copending Application No. 10/779255 do not require the second reagent, the cleavable linkage is cleaved by singlet oxygen (recited in the instant claim 24), it is obvious variation over claims 21-30 of copending Application No. 10/828647 to add the second reagent to the composition for the instant claims. Moreover, both sets of claims require the electrophoretic probe, which is defined by the same formula. Thus, the obviousness-type double patenting rejection is applicable.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Claims 21-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,770439. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 21-30 are drawn to a composition comprising a set of electrophoretic probe and a second reagent which is capable of generating an active species, singlet oxygen (recited in claim 30) to cleave the cleavable linkage, while claims 1-7 of U.S. Patent No. 6,770,439 are drawn to a set of specific binding pairs comprising a first reagents and second reagents in which the first reagent is defined by the same formula as the electrophoretic probes of instant claim 21 and the second reagent which has the same function as the second reagent claimed in claim 21. Thus it is obvious variation over claims 1-7 of U.S. Patent No. 6,770,439 to make a composition with the set of binding pair of claims 1-7 of U.S. Patent No. 6,770,439. Moreover, both sets of claims

require the electrophoretic probe, which is defined by the same formula. Thus, the obviousness-type double patenting rejection is applicable.

4. Claims 21-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 70017125. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 21-30 are drawn to a composition comprising a set of electrophoretic probe and a second reagent which is capable of generating an active species, singlet oxygen (recited in claim 30) to cleave the cleavable linkage, while claims 1-13 of U.S. Patent No. 7,001,725 are drawn to a kit comprising a plurality of electrophoretic probes and a second reagent. The electrophoretic probes of claims 1-13 of U.S. Patent No. 7001725 have the same structure as the electrophoretic probe of the instant claims. The second reagent of claims 1-13 of U.S. Patent No. 7001725 also has the same function as the second reagent of the instant claim. Thus it is obvious variation over claims 1-13 of U.S. Patent No. 7,001,725 to make the composition, instead of making the kit of claims 1-13 of U.S. Patent No. 7,001,725. Therefore, the obviousness-type double patenting rejection is applicable.

5. Claims 21-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6673550. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 21-30 are drawn to a composition comprising a set of electrophoretic probe and a second reagent which is capable of generating an active species, singlet oxygen (recited in claim 30) to cleave the cleavable linkage, claims 1-20 of US patent No. 6673550 are drawn to a probe set which is defined by the same formula as recited in the instant claim 21. The differences

between these claims are that claims 1-20 of US patent No. 6673550 recite more specific chemical group for the detection group D that is a fluorescent molecule and do not recite a second reagent which is capable of generating an active species, singlet oxygen (recited in instant claim 30) to cleave the cleavable linkage. However, claims 1-20 of US patent No. 6673550 require an active species to cleave the cleavable linkage in claim 1. Thus the instant claims and claims 1-20 of U.S. Patent No. 6673550 are related as genus-species. Therefore, the obviousness-type double patenting rejection is applicable.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 21-30 are vague and indefinite because it is unclear what is encompassed by the phrase "aggregation".

b. Claim 30 is vague and indefinite because claim 30 can depend on itself. It is suggested to correct the dependency.

c. Claims 26-30 are vague and indefinite because the phrase "said plurality" has no antecedent basis.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 21-22, 24, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Grossman et al. (US 5,470,705, issued November 28, 1995).

Grossman et al. disclose a probe composition of detecting a plurality of different sequences in a target sequence involving a plurality of sequence probes (See column 2, lines 54-64 and column 6, lines 46-54). The number of the probes is six probes, which are added to a target polynucleotide (See column 20, lines 49-51). The probe used in the method has the features of the electrophoretic probe cited in the instant claim 21. The probe includes a binding polymer, a polymer chain that imparts to that probe, a distinctive ratio of charge/translational frictional drag and a reporter attached to the binding polymer (See column 20, lines 52-57). The binding polymer is an oligonucleotide including at least 10-20 bases allowing hybridization to the target polynucleotide (See column 6, lines 66-67 and column 7, lines 1-10). Other binding polymers are analogs of polynucleotides, such as deoxynucleotides with thiophosphodiester linkage (See column 7, lines 11-19). The polymer chain has a ratio of charge/translational frictional drag, which is evidenced by a distinctive electrophoretic mobility in a non-sieving matrix (See column 7, lines 50-64). The polymer chain can be polyethylene oxide (PEO) or a polypeptide chain where the chains are attached to different-sequence binding polymers (See column 3, lines 11-18). The teachings suggest that the charge/translational frictional drag is consisted of carbon, hydrogen, oxygen, phosphorus, nitrogen, sulfur and boron.

The second reagent is not defined in the claim. However, Grossman et al. disclose that the probe is cleaved by 5'to 3' exonuclease (See column 20, lines 15-25). The exonuclease is

interpreted as the second reagent, which is capable of generating an active species to cleave the cleavable linkage.

Moreover, since the aggregation is not defined, the features of Grossman et al.'s probe has the features of the claimed electrophoretic probe, the teachings of Grossman et al. anticipate the limitations of the claims.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11 Claims 21-25, 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al. (6,027,890) in view of Grossman et al. (US 5,470,705, issued November 28, 1995).

Van Ness et al. disclose a variety of first and second member of a ligand pairs in which one or more members used in the method is tagged (See column 2, lines 14-27) and the tag is cleavable by oxidation (See column 4, lines 16-24). The ligand pair can be an antibody or

antibody fragment or nucleic acid molecule/nucleic acid molecule (See column 2, lines 29-44). The tag is detectable by non-fluorescent spectrometry, or potentiometry (See column 2, lines 55 to column 3, lines 1-8) or the tag can be fluorescent labeled and detected by fluorometer (See column 3, lines 37-40). The labile linking group has thioethers, disulfide formation (See column 37, lines 12-26) and sulfoxide (See column 34, lines 39-46). There are more than 500 different and unique tagged molecules and each tag is unique for a selected nucleic acid fragment or first or second member and may be separately identified (See column 3, lines 29-36). The bound member and unbound member are separated by electrophoresis (See column 3, lines 58-67). The member ligand pair of Van Ness has the same components of the probe set.

However, Van Ness et al. do not disclose the ligand pair having a mobility modifier, which produces a unique electrophoretic mobility.

Grossman et al. disclose that the probe includes a binding polymer, a polymer chain which imparts to that probe, a distinctive ratio of charge/translational frictional drag and a reporter attached to the binding polymer (See column 20, lines 52-57). Grossman et al. also disclose that a ratio of charge/translation frictional drag is distinctive for each different-sequence probe in which addition of charge groups to the polymer chain or the subunit length of the polymer chain can be used to achieve selected ratio of charge/translation frictional drag (See column 11, lines 34-43) and the electrophoretic movement in a non-sieving medium can finely resolved by derivatization with polymer chain having slightly different size and /or charge differences (See column 11, line 46-51).

One of ordinary skill in the art would have been motivated to apply the mobility modifier of Grossman et al., the ratio of charge/translation frictional drag to the ligand pair of Van Ness et al. because as taught by Grossman et al. the ratio of charge/translation frictional drag is distinctive for each different-sequence probe and the electrophoretic movement in a non-sieving medium can finely resolved by derivatization with polymer chain having slightly different size

and /or charge differences (See column 11, line 46-51). It would have been prima facie obvious to have the mobility modifier in the ligand pair of Van Ness et al. to make the claimed probe in the composition.

12. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705, issued November 28, 1995).

The teachings of Grossman et al. are set forth in section 9 above. Grossman et al. do not disclose the molecular weight of the mobility modifier.

Grossman et al. disclose a probe composition of detecting a plurality of different sequences in a target sequence involving a plurality of sequence probes (See column 2, lines 54-64 and column 6, lines 46-54). The number of the probes is six probes, which are added to a target polynucleotide (See column 20, lines 49-51).

Grossman et al. do not explicitly disclose the molecular weight of the mobility modifier. However, the binding polymer and polymer chain contribute to the mobility modifier of probe (See column 3, lines 55-64,). The polymer chain may be polyethylene oxide (PEO) or a polypeptide chain (See column 3, lines 11-18, column 7, lines 39-49). Since these molecules are small molecules, the teachings are inherent that the molecular weight of the mobility modifier would be from 150-5000 Daltons.

One of ordinary skill in the art would have been motivated to apply the molecule weight of binding polymer and polymer chain used in the method of Grossman et al. because Grossman et al. disclose that the binding polymer and polymer chain contribute to the mobility modifier of the probe (See column 3, lines 55-64), the mobility modifier is distinctive for each different-sequence probe (See column 11, lines 34-43) and the electrophoretic movement in a non-sieving

medium can finely resolved by derivatization with polymer chain (See column 11, line 46-51). It would have been prima facie obvious to apply the mobility modifier with the molecular weight in the range of from 30-3000 daltons to make the probe in the composition.

13. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman et al. (5,470,705, issued November 28, 1995) as applied to claims 21-22, 24 26 and 28 above, and further in view of further in view of Breslow et al. (6,331,530, issued Dec 18, 2001).

The teachings of Grossman are set forth in section 9. None of the references addresses the cleavable linkage, which is cleaved by singlet oxygen.

Breslow et al. disclose a linker between two β-cyclodextrin molecules and that a photosensitizer is encapsulated within a matrix, wherein the cleavable linker is cleaved upon exposure to light (See the abstract). Singlet oxygen is produced to cleave the linker (See column 3, lines 47-51).

One of ordinary skill in the art would have been motivated to apply the cleavable linker, which is cleaved upon exposure to light because the active cleaving agent, singlet oxygen is used in the system of Breslow et al. for cancer therapy and this suggests that the active cleaving agent must be very efficient. Thus, it would have been prima facie obvious to apply the cleavable linker, which is cleaved by singlet oxygen as taught by Breslow et al. to make the claimed probe set.

Summary

14. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joyce Tung
June 3, 2006

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

6/8/06